ALBERTA HERITAGE FOUNDATION FOR MEDICAL RESEARCH

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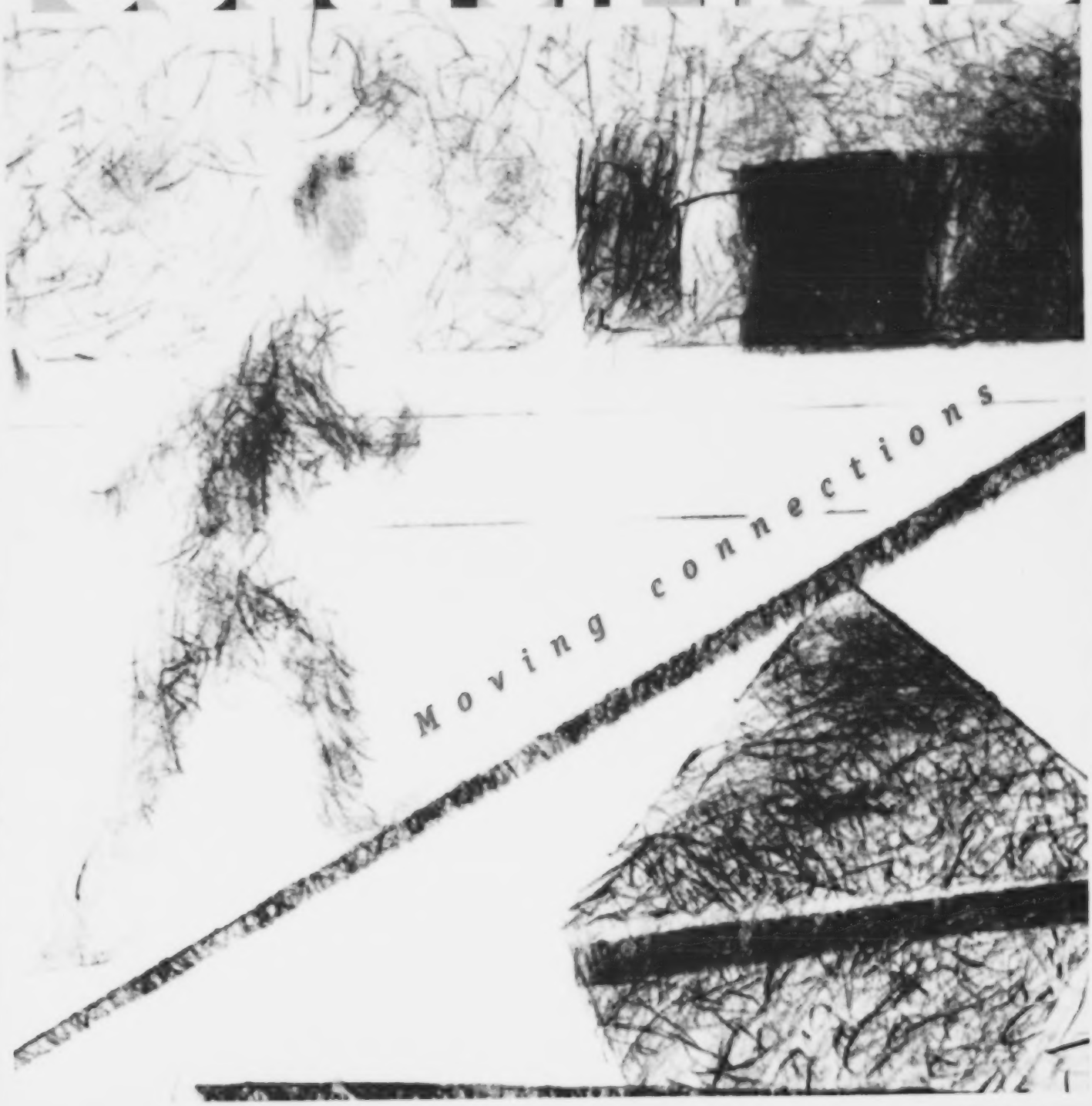
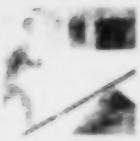
SUMMER 2008



Moving connections

On the Cover



Chris Judge is an Edmonton artist living with multiple sclerosis (MS). He received his MFA from the University of Victoria in 1988 and taught at Sir Wilfred Grenfell College, Memorial University, in Corner Brook, Newfoundland for several years. Chris has had many exhibitions of his work throughout Canada and the US. His work is represented by Lando Fine art at www.landofineart.com/judge. *Steep Sidewalks* is a 2002 coloured drawing.

research news

ALBERTA HERITAGE FOUNDATION FOR MEDICAL RESEARCH

SUMMER 2003

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Medical geneticists examine specific genes for mutations that may cause disease.

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AHFMR Mission

AHFMR supports a community of researchers who generate knowledge whose application improves the health and quality of life of Albertans and people throughout the world. AHFMR's long-term commitment is to fund health research based on international standards of excellence and carried out by new and established investigators and researchers in training.

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Research Vie

Traditionally, physicians have kept up to date with the latest advances in medical science by reading weekly or monthly periodicals. More recently, many of these print medical and scientific journals have gone online as well. The Boston-based *New England Journal of Medicine* has published since 1812 and has established itself as one of the most prestigious medical journals in the world. On a recent AHFMR-sponsored visit to Edmonton, editor-in-chief Dr. Jeffrey M. Drazen discussed how the journal raced the clock to get new research about severe acute respiratory syndrome (SARS) on its Web site as quickly as possible during the initial outbreak.

The international outbreak of SARS this spring showed just how big a role the Internet and e-mail now play in communicating timely medical information. Medical professionals around the world kept each other up to date via e-mail, and public health authorities kept the public informed through their Web sites. Even the venerable *New England Journal of Medicine* published new SARS research on its Web site only days after receiving submissions from doctors in Toronto and Hong Kong who were working in the middle of the public health storm.

The authors and the journal worked overtime to get the papers out in just eight days without skipping any steps in the journal's tough editorial and peer-review process. Normally it takes about 12 weeks to get an article published. "We felt that these were important things for physicians to know of right away," says Dr. Drazen. "To know what SARS looked like—medically, not what they could read in the newspaper. And so we worked very hard to get papers up and out in a very timely fashion."

SARS showed just how big a role the Internet and e-mail now play in communicating timely medical information.

The SARS papers arrived in the office on March 23 and the first two papers were published on the Web (after being reviewed by six people and revised five or six times) on March 31. There were 700,000 downloads of the articles in the first two weeks—a record for the publication. "We thought that this was medically useful information," Dr. Drazen says. "It was at a time in the SARS epidemic where rapid case recognition and treatment was critical to putting the brakes on the epidemic." All the SARS research articles eventually came out in the May 15 print version of the *New England Journal of Medicine* as well, along with a number of related commentaries.

Throughout the process, most communications between the journal, the authors, and the reviewers took place electronically. "It wouldn't have happened without e-mail and the Internet," Dr. Drazen says. "It would have been impossible 10 years ago."

While the journal's comprehensive review process was fast-tracked to deal with the overwhelming demand for information during the SARS outbreak, the editors still followed every step to make sure the SARS papers were up to the journal's high standards.

Dr. Drazen expects 4,500 submissions to the New England Journal of Medicine this year and as editor-in-chief, he will flip through every single one of them. Papers warranting a closer look are either passed on to eight associate editors, who review them in more detail, or sent to outside experts for review. The editors then meet as a group, to hash out which of these papers will actually be published. Papers that make the cut receive a technical review for aspects such as statistical analysis and methodology, and are sent back to the author for revisions. An in-house copy-editor then dissects the papers to make sure the writing is up to the journal's standards. Dr. Drazen has final say on every paper. In the end, fewer than one in ten papers submitted to the journal are published.

ABOVE: DR. JEFFREY M. DRAZEN

Making connect

Alberta's health-service professionals have many good ideas on how to improve patient and client care and better manage healthcare resources. But busy rural physicians might be stretched too thin on time and research resources to test their ideas. Or suppose you're a nurse, a rehabilitation therapist, a social worker, a health-service manager or health economist, and you have a bright idea for a project. How do you research it if you're not sure where to start?

Supported by Heritage funding, the Alberta Consultative Health Research Network (ACHRN) is enhancing regional capacity to carry out research studies, evaluation projects, and research utilization initiatives. Dr. Bonnie Dobbs at the University of Alberta and Dr. Brad Hagen at the University of Lethbridge are ACHRN's first research development advisors. AHFMR funding enabled the network to hire Dr. Dobbs and Dr. Hagen on a part-time basis for three years, starting in September 2002. These two medical researchers are the "point persons" in building new research partnerships between health-service professionals and academic medical scientists. "Many healthcare professionals want to incorporate research into their everyday practice," explains Dr. Dobbs, "but it's just finding the time to do it, or not having the expertise to do it. That's where we come in."

Dr. Hagen cites one project that involved the former Headwaters Health Authority, which had surveyed junior-high-school students to look at general health issues. With hundreds of survey questionnaires in hand, however, no one in the rural region had the time or expertise to create a computer database of the information, properly analyze it, and disseminate the findings. Dr. Hagen was able to link the people in the Headwaters region with a researcher at the University of Lethbridge School of Health Sciences, who was interested in the same topic. Together, they obtained the expertise to create the database and do some statistical analysis. The partners will present the survey findings to school boards, and they will also likely collaborate on publishing the research.

ACHRN was formed in January 1999 in response to the long-recognized need to provide consultation and training services for health-service professionals in Alberta. These front-line health workers are directly involved in delivering the best possible care to patients and clients, and are often in an ideal position to see how quality and cost-efficiency of care could be improved. The scientific means to validate ideas is to do some research. Through ACHRN, health professionals can increase their skills and boost their confidence in the care they provide, Dr. Dobbs says. "I think anytime you incorporate evidence into your practice—as long as you're incorporating the right evidence—the outcomes have to be positive."

Academic medical researchers, on the other hand, are typically involved in major research projects, for which they have to secure funding and then build a research team; and once the projects are underway, there is the ongoing process of publishing their work. "They don't necessarily always see the advantages of involving clinical people with their research projects or their grants," says Dr. Hagen. But clinical input can broaden and strengthen the scope of a research proposal; and the link with direct clinical practice can yield valuable opportunities to co-publish the findings with clinical practitioners.

Edmonton, Calgary, and Lethbridge, with their university schools of medicine or health sciences,

>>> How do you research it if you're not sure where to start?

ions for research

already have well-connected research infrastructures. However, academia is not the only setting where research ideas are being generated. Rural health-service professionals are usually very knowledgeable about the health priorities and needs of their particular communities. They stand to benefit from connections with professionals in other regions who are dealing with similar issues.

"What we're trying to do is support the health region people who are trying to solve those day-to-day problems, by doing some relatively small research projects," Dr. Hagen says. "The goal," adds Dr. Dobbs, "is to have Brad and me act as a liaison between people in the community and academic researchers, so that we can help them build partnerships."

"I can see research being done that actually solves some real-world problems."

A nurse by training, Dr. Hagen does a lot of medical research; he also teaches research to students in the nursing program and the addictions counselling program in the University of Lethbridge's School of Health Sciences. "One particularly satisfying aspect of being an ACHRN research development advisor is that I can see research being done that actually solves some real-world problems," he says.

Dr. Dobbs, whose job at the University of Alberta's Rehabilitation Research Centre involves promoting and facilitating research on campus and in the community, does similar work for ACHRN. From March to May, she presented workshops in small communities in Alberta's East Central Regional Health Authority, for health professionals who want to learn how to incorporate evidence-based findings in their practice. "The greatest satisfaction for me, being a researcher, is providing clinicians with the tools to use research to make decisions," Dr. Dobbs says.

"The greatest satisfaction for me is providing clinicians with the tools to use research to make decisions."

ACHRN's services, usually provided free of charge, include support for research proposal and grant application preparation; research design; data collection, management analysis and presentation; applied research; health policy planning, management, and organization; and research dissemination and transfer.

Network director Dr. Kerrie Pain of the University of Calgary's Department of Community Health Sciences says that ACHRN plans to add two more research development advisors by September 2003. "The goal is to have a total of five RDAs by the end of 2004, so that we can create closer linkages with professionals in the different geographic areas of Alberta," she explains.

Dr. Bonnie Dobbs is an Assistant Professor in the University of Alberta's Faculty of Rehabilitation Medicine and Adjunct Professor in the Department of Psychology. She is also Associate Director of the Rehabilitation Research Centre at the University of Alberta.

Dr. Brad Hagen is an Associate Professor in the School of Health Sciences at the University of Lethbridge.

LEFT: DR. BRAD HAGEN ABOVE: DR. BONNIE DOBBS

MEDICAL GENETICS

a very fundamental level

As a graduate student, *Heritage Senior Scholar Dr. Moira Glerum was already hooked on studying mitochondrial diseases. However, she never anticipated that research done so early in her career would have such an immediate application.*

At the time, Dr. Glerum was doing basic research using a cell line from a child who had died of Leigh syndrome. This mitochondrial disease, characterized by progressive neurological deterioration, usually appears in the first year of life and is generally fatal in the first decade. There is no cure. The child's mother had kept in touch with Dr. Glerum's supervisor, Dr. Brian Robinson at Toronto's Hospital for Sick Children. She knew the disease was inherited and so had decided not to have any more children (the child who died was her first). Dr. Glerum was able to identify the biochemical defect that caused the disease, and alert the woman that the defect could be detected by prenatal testing. The woman has since had two healthy children.

"This was a formative experience for me," says Dr. Glerum. "It showed how basic research in medical genetics can truly help people. It's one of the reasons I'm doing this work."

Dr. Glerum is continuing her research into mitochondrial diseases at the University of Alberta. Mitochondria are the tiny energy factories found inside almost all our cells. A mitochondrial disease can shut down some or all of the mitochondria, cutting off this essential energy supply. It is thought that defects in mitochondrial function may be the most common underlying cause of many neurodegenerative diseases, and mitochondria are believed to play a role in Parkinson's and Alzheimer's diseases.

Dr. Glerum's work focuses on cytochrome oxidase (COX), one of the key proteins required for mitochondrial formation. One of the largest subgroups of mitochondrial diseases is caused by COX defects.

"Basic research in medical genetics can truly help people."

"Proteins are assembled in beautiful, intricate pathways in the mitochondria," says Dr. Glerum. "But at any point something can go wrong. In most cases, the consequences are devastating."

Understanding these pathways is the aim of Dr. Glerum's research. Her experiments are done in yeast, where she can "knock out" various genes and investigate the effects on the mitochondria. She has identified the protein sequence for a number of previously unknown COX assembly factors. Other researchers have then taken these results, sequenced the genes in humans, and found the mutations that cause COX defects.

"Studies on yeast might seem very removed from human disease, but it's only because of the work in yeast that we've been able to understand what's going on at the molecular level," explains Dr. Glerum. "Applying this knowledge will ultimately help many people."

Repairing damaged genes

Alberta-based medical genetics researchers like Dr. Glerum are working on a number of other exciting projects aimed at uncovering the genetic basis of a wide variety of diseases. For example, Heritage Scholar Dr. Susan Andrew is studying the instability of DNA and how it relates to human disease. Her particular interest is the role certain proteins play in fixing mistakes in DNA.

"DNA mismatch repair proteins are like a spell checker for your genes," explains Dr. Andrew. "Their main job is to repair mistakes in the DNA sequence so that each new cell receives a correct set of genes. A whole array of proteins carry out this DNA surveillance. I want to understand how they do it."

One way to study this is to look at a disease where DNA mismatch repair is not working well. When a mutation—an error within the genes of a cell—is present in one of the mismatch repair genes, the spell-checking function goes awry and mutations in other genes are allowed to persist. Such is the case in individuals with hereditary non-polyposis colorectal cancer—the most common form of inherited colon cancer, accounting for up to 5% to 10% of all colon cancers.

"This disease is a dramatic example of how the persistence of mutations can lead to uncontrolled growth and eventually to cancer," says Dr. Andrew. "But we now know that a significant number of other cancers show some degree of DNA instability. There's real urgency in knowing more about the repair pathways."

Dr. Andrew's cancer research has led to a collaboration with skin cancer expert Dr. Victor Tron, Professor and Chair of the University of Alberta's Department of Laboratory Medicine and Pathology. Their hypothesis is that the DNA mismatch repair proteins act as sensors for DNA damaged by ultraviolet light. Their research indicates that in some cases the proteins can go beyond the DNA **Page 6 ▸**

"DNA mismatch repair proteins are like a spell checker for your genes."

ABOVE: DR. MOIRA GLERUM

DR. SUSAN ANDREW

repair function, signalling to other proteins to initiate another pathway that actually destroys the affected cell. In some cases of skin cancer, this signalling capability may be defective.

"DNA mismatch repair proteins may play a more global role than repair alone," says Dr. Andrew. "If we can understand these pathways, it may be possible to restore the ability to kill damaged cells, and thus stop the development of cancer."

Preventing birth defects

Heritage Scholar Dr. Alan Underhill studies neural tube defects, such as spina bifida, which are caused by the failure of the fetus's neural tube to close properly during the very early stages of pregnancy. These disorders lead to incomplete development of the brain and spinal cord.

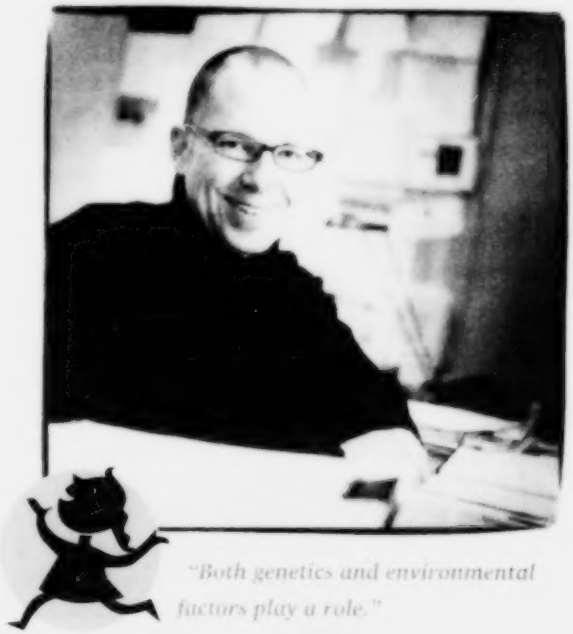
"It's difficult to understand how these defects happen, because both genetics and environmental factors play a role," says Dr. Underhill. However, genetics researchers are making some inroads. "Over the past 10 years, more than 80 genes have been identified that, when knocked out, result in a neural tube defect. And we don't know all the genes yet," he continues. "The complexity is more than anyone thought."

Dr. Underhill studies a gene called Pax3, which exists in mice and humans and is normally only expressed during development. Mutated versions of this gene are implicated in neural tube defects, as well as in Waardenburg syndrome, an inherited condition characterized by malformed facial bones, pigmentary disturbances such as two different coloured eyes, and deafness. These disorders are caused by a failure of the gene to function during development. Interestingly, Pax3 is re-activated in melanoma, the most lethal type of skin cancer.

"So Pax3 may be a possible point of intervention for melanomas," says Dr. Underhill. "In cell culture, it has been demonstrated that if you turn the gene off, melanoma cells will stop dividing and eventually die.

"This is promising, but it's important to note that genes are only an entry point into a pathway. We're trying to better understand these pathways once the gene has provided the place to start.

"I enjoy exploring this kind of uncharted territory—describing how processes work at a very fundamental level. If we can understand how Pax3 works and contributes to birth defects and cancer development, then we can begin to define new therapies and treatments for these conditions."



"Both genetics and environmental factors play a role."

Dr. Moira Glerum is a Heritage Senior Scholar and an Associate Professor in the Department of Medical Genetics at the University of Alberta. She is also a Principal Investigator with the Canadian Genetic Diseases Network. Her research is also supported by the Canadian Institutes of Health Research (CIHR), Canada Foundation for Innovation and NSERC (the Natural Sciences and Engineering Research Council).

Dr. Susan Andrew is a Heritage Scholar, a CIHR Scholar, and a Canadian Genetic Diseases Network Scholar. Her research is also supported by the National Cancer Institute of Canada; the Alberta Cancer Board; the University Hospital Foundation; and the Cancer Research Society. Dr. Andrew is an Assistant Professor in the Department of Medical Genetics at the University of Alberta.

Dr. Alan Underhill is a Heritage Scholar and an Assistant Professor in the Department of Medical Genetics at the University of Alberta. His research is also supported by CIHR and the Alberta Cancer Board.

Recent publications

Punter FA, Glerum DM. Mutagenesis reveals a specific role for Cox17p in copper transport to cytochrome oxidase. *Journal of Biological Chemistry* 2003. In press 2003.

Whiteside D, McLeod R, Graham G, Steckley JL, Booth K, Somerville MJ, Andrew SE. A homozygous germ-line mutation in the human *MSH2* gene predisposes to hematological malignancy and multiple café-au-lait spots. *Cancer Research* 2002 Jan 15;62:359-362.

Kibar Z, Vogan KJ, Groulx N, Justice MJ, Underhill DA, Gros P. *Ltap*, a mammalian homolog of *Drosophila Strabismus/Van Gogh*, is altered in the mouse neural tube mutant Loop-tail. *Nature Genetics* 2001 July;28:251-255.

ABOVE: DR. ALAN UNDERHILL

Medical genetics is the study of normal variations in genes and the abnormal changes (mutations) which lead to medical illnesses and disorders. Medical geneticists examine specific genes from individuals for mutations that may cause disease. However, to get an accurate picture of the effects of these genes and to predict the occurrence and costs of disease, they must sometimes look at the genes across a larger population. To do so, they need complex statistical tools and methods to analyze their data.

GENETIC MAPMAKING

Enter Dr. Bruce Rannala, who works in an area called mathematical population genetics. Using computers and statistics, Dr. Rannala develops programs and techniques to map the position of disease mutations. One such program now has several hundred registered users from around the world who use it for fine-scale gene mapping of particular diseases.

Dr. Rannala is also involved in a joint initiative of the CIHR institutes of Genetics and of Population and Public Health to design the Canadian National Birth Cohort Study. Many countries are now collecting large population samples of DNA from hundreds of thousands of individuals, to look at incidences of common genetic disorders and then map the genes associated with these disorders.

"The big push in genetics right now is common disorders such as asthma, hypertension, and type 2 diabetes," Dr. Rannala explains. "These types of disorders have a genetic component–and many different genes could predispose for the condition–but there is also a large environmental component. This kind of complexity makes the mutations much more difficult to map."

The proposed Canadian study would involve collecting DNA from a group of people at birth, and then examining factors such as environmental exposures over the course of their lives and trying to put together the associations. The steering committee, composed of both geneticists and epidemiologists, is choosing entire families to sample–30,000 families, consisting of approximately 90,000 individuals. The idea of this unique design is to study transmission of genes within families as well as the associations across families.

The idea is to study transmission of genes within families as well as the associations across families.

A biologist by training, Dr. Rannala explains that when he was an undergraduate, population genetics was very descriptive and theoretical. "This was about the time that the genome sequence project was just getting started, so there was not yet a lot of human data to work with."

He points out that the broad interdisciplinary training in both math and biology required to be a mathematical population geneticist makes it a fairly rare discipline. "Most of my students come from a biology background but then spend a lot of time taking statistics and computer science courses," says Dr. Rannala. "I find it easier to teach biologists mathematics than to teach mathematicians biology."

Dr. Bruce Rannala is a Heritage Scholar and an Associate Professor in the Department of Medical Genetics at the University of Alberta. He also receives funding from the CIHR and the National Human Genome Research Institute (NIH).

Recent publications

Rannala B. Finding genes influencing susceptibility to complex diseases in the post-genome era. *American Journal of Pharmacogenomics* 2001;1(3):203-221.

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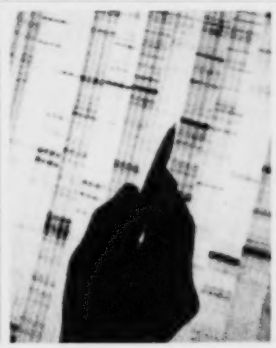


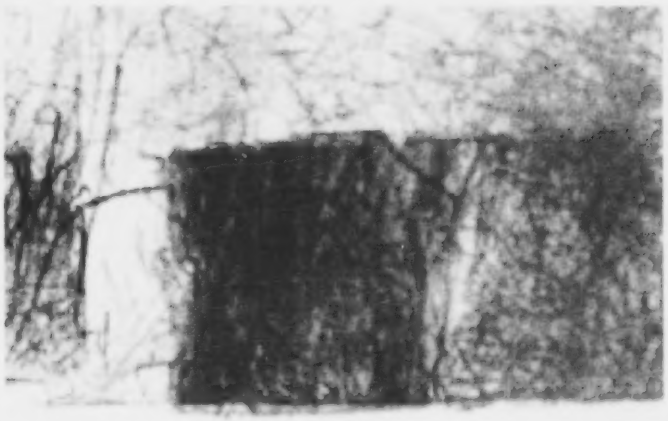
ABOVE: DR. BRUCE RANNALA

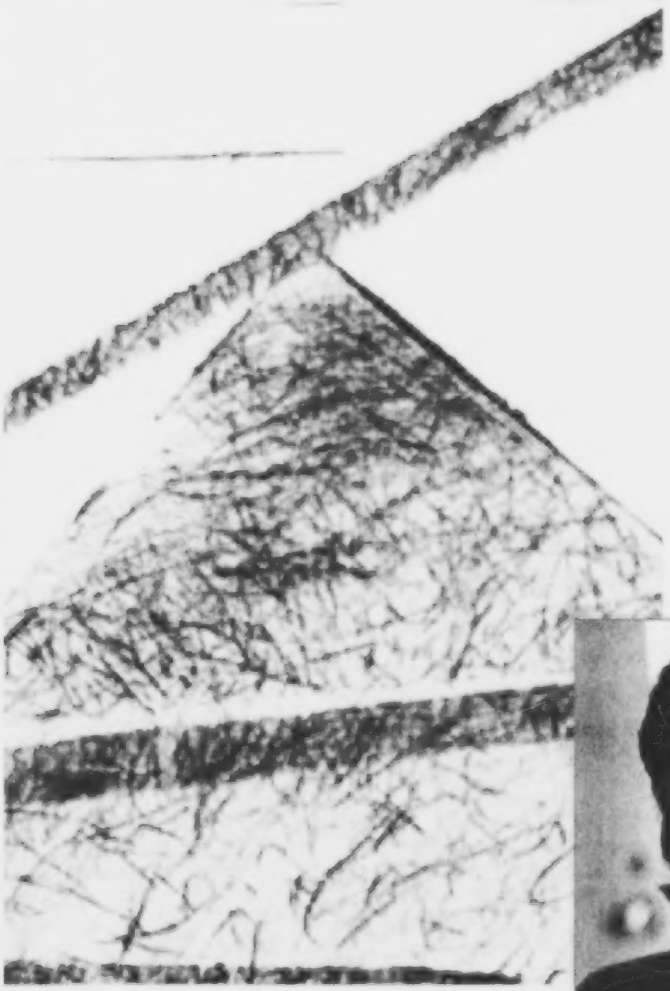
Restoring movement

Most of us take movement for granted—

standing, walking, reaching, grasping, and even sitting upright are functions that we perform countless times a day, usually without a second thought. Loss of movement and function from injury or disease can be a devastating experience. With support from AHFMR, researchers in Alberta are using a variety of approaches to restore movement for people suffering from conditions which affect the nervous system, such as spinal cord injury, stroke, Parkinson's disease, and multiple sclerosis. >>>

after nerve injury





There are close to 300,000 people living with spinal cord injuries in North America, and 11,000 new injuries every year. Unlike any other neurological injury, spinal cord injury is most common in young people, those 15 to 35 years old. Major medical advances have already been made in improving the chances of survival for these individuals, and scientists are trying to find ways to improve their quality of life as well.

Tiny wires in the spinal cord

One of these scientists is Heritage Scholar Dr. Vivian Mushahwar at the University of Alberta. Dr. Mushahwar is working on a new variation of something called functional electrical stimulation—applying electrical currents to generate activity in the nervous system which would result in muscle contraction and limb movements. Various electrical stimulation systems have been in existence for nearly 100 years.

Dr. Mushahwar is focusing on a means of stimulating the spinal cord itself rather than stimulating specific nerves. Using a technique called intraspinal microstimulation (ISMS), she implants tiny, hairlike wires into the lumbar region of the spinal cord. This small area of the lower back—about 5 centimetres long—contains the cell bodies that control leg movements. By passing electrical pulses through these wires, Dr. Mushahwar has been able to induce controlled limb movements similar to normal walking. "Our preliminary experiments indicate this may be a safe technique to restore leg movements," she says.

In collaboration with Heritage Scientist Dr. Arthur Prochazka, Dr. Mushahwar is also looking at using the ISMS technique to restore bladder and bowel movement and sexual function. "Locomotion is the most visible need, but there are a number of other functions such as these that take even higher priority for people with spinal cord injury," she explains. **Page 10 ▸**

DR. VIVIAN MUSHAHWAR

Muscle contraction

Also at the University of Alberta, Heritage Scholar Dr. David Collins works with electrical stimulation to make muscles contract, using electrodes that stick to the surface of the skin and stimulate the muscle directly underneath. While doing his post-doctoral work in Australia, he started experimenting with stimulation at higher frequencies and longer pulses. Contrary to previous work with electrical stimulation, he found that the force began to increase about a second after the stimulation was turned on, and sometimes the muscle stayed contracted after it was turned off. Trying to determine where this extra force was coming from, Dr. Collins realized that reflexes were triggering nerves within the spinal cord (the same ones that Dr. Mushahwar stimulates directly with ISMS). These nerves (motoneurons) were being turned on indirectly by signals coming from the sensory nerves located under the stimulating electrodes.

Dr. Collins realized that reflexes were triggering nerves within the spinal cord.

"Until recently, it was thought that these motor nerve cells or neurons simply did as they were told," Dr. Collins explains. "My work suggests that these neurons go into a different state, called a plateau potential, and that they are much more actively involved in controlling movement than was previously thought. Sometimes they flip into this other state, where they continue firing even though they are getting no input."

Part of Dr. Collins' research is investigating to what extent the neurons show these plateau potentials, and whether plateau potentials contribute to normal movements when there is no electrical stimulation. "We're triggering some mechanism within the central nervous system that's coming back out to the muscles and setting off a much larger contraction," he says. "We want to investigate to what extent we can trigger this mechanism and whether it can be triggered reliably. Can we bring about this effect in spinal-cord-injured and stroke patients?" Dr. Collins hopes that the technique can be used to boost contractions brought about by more traditional functional electrical stimulation technology.

Dr. Collins has also worked with Dr. Prochazka and Dr. Mushahwar and is considering future collaborations. "Edmonton is one of the best places to do this kind of work," he says. "Not only is there an established group of people, but there are also a lot of up-and-coming scientists."

Deep brain stimulation

At the University of Calgary, Heritage Clinical Investigator Dr. Zelma Kiss works with a very different type of electrical stimulation, one that has applications for patients with Parkinson's disease and tremor rather than spinal cord injury. Deep brain stimulation (DBS) involves surgically implanting a wire device into the patient's brain. The device is connected to a stimulator which is implanted in the upper chest and which can be turned on or off by the wearer. The stimulator produces an electric current which is sent along to the electrode implanted in the brain, which it stimulates to block the patient's muscle tremor, allowing normal movement. The technology is similar to that of a pacemaker. In use since the 1970s to relieve pain, DBS was adapted in the 1990s for movement disorders such as Parkinson's disease and tremor, with excellent results.

In spite of the fact that this technology has been in use for some 30 years, how it works and what happens to the cells near where the stimulation is taking

DBS involves surgically implanting a wire device into the patient's brain.

ABOVE: DR. DAVID COLLINS BOTTOM RIGHT: DR. ZELMA KISS TOP RIGHT: DR. KARIM FOUAD

place is still not clearly understood. Dr. Kiss, a neurosurgeon who implants these devices in her own patients, uses a microelectrode to record and amplify the electrical signals in the patient's brain. This allows her to develop a three-dimensional map prior to placing the DBS electrodes in the correct brain site. The patients are awake and co-operative as this is happening and can describe whether they feel any sensation such as tingling. "We can change our electrical stimulation parameters to try to figure out what parts of a cell may be activated," Dr. Kiss explains. "We change the pulse durations of the stimuli and ask the patients when they actually feel tingling. It's tremendously helpful in terms of helping us understand how the electrical stimulation is working. Is it working on the bodies of the cells? Is it working on the fibres? Which part of the cell is being primarily affected?"

The patients go through complete assessments and follow-up 6 months after surgery and then every year after that. "We're also still learning how long this lasts and whether this form of treatment can bring about long-term changes in brain function," says Dr. Kiss. By combining data collected from patients participating in other experimental studies, her team is gradually unravelling the processes involved in DBS. This understanding could allow DBS to be applied to a variety of other conditions such as other movement disorders, epilepsy, and even psychiatric conditions such as obsessive-compulsive disorder.

Dr. Fouad is working on what he calls his "dream project".

Regeneration

With AHFMR funding, University of Alberta Heritage Scholar Dr. Karim Fouad is working on what he calls his "dream project"—a combination of treatments to bring about recovery of movement after spinal cord injury by regenerating nerve cells.

When the spinal cord is injured, its neurons or nerve cells face several obstacles that prevent them from growing back: the injured spinal cord has cavities, empty spaces in which neurons cannot grow; the scar caused by the injury hinders the neurons; and the white matter of the spinal cord is filled with proteins that act as stop signs to regenerating neurons. Dr. Fouad tackles these obstacles one by one. **Page 12 ▸**

ARTWORK: CHRIS JUDGE. *DANCING WITH A FRIEND*, 2003. COLOURED PENCIL.

First, he fills the cavities with cells from peripheral nerves (those that branch out from th spinal cord to the rest of the body); since peripheral nerves have the ability to regenerate, these cells permit the spinal cord neurons to grow. He also adds cells called olfactory ensheathing glial cells, which offer a bridge for the regenerating neurons through the hostile environment. Dr. Fouad then applies an enzyme to the lesion site to digest the scar tissue. Finally, he neutralizes the "stop sign" proteins with antibodies.

"We put this all together through surgery and then see what happens," he explains. "We look to see whether the neurons actually regenerate and whether there is recovery of locomotion. The ultimate test is whether it all reconnects properly to motoneurons that then activate the muscles."

"I am between two fields," Dr. Fouad says. "Most people studying regeneration are molecular scientists—molecular biologists or biochemists, for instance. They come up with the methods to promote regeneration. On the other side are the people who study physiology and how locomotion is controlled. I try to bridge both groups and take this into a meaningful model."

Regeneration of brain cells

University of Calgary Heritage Scientist Dr. Sam Weiss is also working toward restoring movement through regeneration of cells, but in the movement control centre—the brain itself.

In 1992, Dr. Weiss made headlines with the discovery of the existence of stem cells in the adult brain which were very similar to those in the developing brain. The discovery was significant on many levels, but especially because it would allow scientists to move toward learning how to stimulate these cells to repair the brain. In his 11 years of work since, Dr. Weiss has discovered that the normal role of these stem cells is to continuously replenish the part of the brain responsible for our sense of smell. "That understanding has led us to unravel many of the signals that tell the stem cell to make the new brain cells that migrate to this area," he says. "Ultimately, we want to use that knowledge to ask the stem cells to go somewhere else and replenish cells that have been lost due to injury or disease."

Dr. Weiss is working toward regeneration of cells in the brain itself.

DR. SAM WEISS

One of the potential applications for Dr. Weiss's research is stroke, the leading cause of disability in Canada, affecting 50,000 people a year. "In addition to some of the marvellous new therapies that have emerged to prevent the damage that occurs from stroke, we're hoping to contribute innovative ways to repair the brain after a stroke—which just do not exist at present," he explains.

Recently Dr. Weiss has been collaborating with Dr. Bryan Kolb of the University of Lethbridge's Canadian Centre for Behavioural Neuroscience, examining the ability of cells to participate in brain self-repair after stroke. Preliminary results show that stimulating the brain's own stem cells results in both tissue regeneration and functional recovery. Dr. Weiss is also studying how well adult stem cells could serve in repairing brain tissue in Parkinson's disease and multiple sclerosis, as well as collaborating on a project with nine other centres that compares stem cell transplantation with self-repair to see which method works best after stroke.

Adaptation after injury

Also at the University of Calgary, Heritage Scientist Dr. Manuel Hulliger is working on a very different method of restoring movement after nerve injury—not through electrical stimulation or regeneration, but by promoting plastic adaptation, teaching the brain to use different means of accomplishing a given task.

Dr. Hulliger studies the body's complex networks of nerve cells and their role in controlling movements; in particular, the role of sensory feedback mechanisms in the muscles and joints. As a non-invasive means of investigating these systems, he uses vitamin B6 (which is toxic in high doses) to induce a loss of sensation, which in turn leads to a loss of movement in parts of the body. He then examines how the central nervous system adapts.

He explains that this work has demonstrated two major phenom-

ena. "One is that when you have removed as little as about 10% of sensory feedback, as we're doing with the administration of B6, subjects experience devastating motor results and loss of movement. But the second thing is that they can recover to almost normal. The central nervous system can adjust—there is large-scale plastic adaptation occurring here."

Entirely by chance, Dr. Hulliger discovered that the means by which he was testing his subjects was actually contributing to their rehabilitation. Instead of simply having them practice over and over again a simple task such as walking, he tried testing the subjects with challenging motor skill tasks such as walking on narrow beams, over arrays of obstacles, or across a series of pedestals. The results were spectacular.

"Challenging them to new and difficult skills was a stimulus to rehabilitation," he explains. "The rather minor stress involved in performing the unfamiliar motor task may be key to promoting the plastic changes in the nervous system. The challenging behaviour may be activating systems which use adrenalin or similar substances as a neuromodulator (a chemical messenger)." A new approach to neuromotor rehabilitation is now being developed, based on retraining of skills rather than routine movements.

Dr. Hulliger hopes to identify which neuromodulator systems are at work in this adaptation. The idea is that a drug could then be developed to stimulate these systems, in order to facilitate the relearning of motor skills and achieve the same results in patients suffering from peripheral nerve damage due to diabetes or other causes. The discovery could also have major implications for physiotherapists working with stroke patients.

"Multiple approaches are necessary in research, when tackling the unknown," says Dr. Hulliger, summing up the very different methods employed by the many Heritage researchers in diverse fields working to restore movement after nerve injury. "In practice, science is seldom a linear process."

Dr. Hulliger examines how the central nervous system adapts.

Dr. Vivian Mushahwar is a Heritage Scholar and an Assistant Professor in the Department of Biomedical Engineering at the University of Alberta. She also receives funding from the Canadian Institutes of Health Research (CIHR), the Canada Foundation for Innovation (CFI), and the National Institutes of Health (NIH).

Dr. David Collins is a Heritage Scholar and Assistant Professor in the University of Alberta Faculty of Physical Education and Recreation. He also receives funding from CIHR and the Natural Sciences and Engineering Research Council (NSERC).

Dr. Zelma Kiss is a Heritage Clinical Investigator and an Assistant Professor in the University of Calgary's Department of Clinical Neurosciences. She is also a CIHR Phase 1 Clinician Scientist.

Dr. Karim Fouad is a Heritage Scholar and an Assistant Professor in the Faculty of Rehabilitation Medicine at the University of Alberta. He also receives funding from CFI and the International Spinal Research Trust.

Dr. Sam Weiss is a Heritage Scientist and a Professor in the Department of Cell Biology and Anatomy and the Department of Pharmacology and Therapeutics at the University of Calgary. He also receives funding from the Canadian Stroke Network and the Stem Cell Network (Networks of Centres of Excellence), the Multiple Sclerosis Society of Canada, and CIHR.

Dr. Manuel Hulliger is a Heritage Scientist and a Professor in the Department of Clinical Neurosciences at the University of Calgary. He also receives support from CIHR and NIH.

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ABOVE: DR. MANUEL HULLIGER

a milestone for technology commercialization

AHFMR's Technology Commercialization (TC) program is known for funding the development of health-related products in Alberta. This funding is targeted to early-stage companies, ones that still face a long road before their products reach the market. Nonetheless, companies supported by the TC program are showing signs of real progress. In March 2003 the program surpassed the $1 million mark in repayments.

"This is a small step, but a milestone worth celebrating," says Linda Humphreys, AHFMR's Vice President of Corporate Affairs and Commercialization. "Companies we have funded are paying us back from sales and from financing they have attracted."

Launched in 1985, AHFMR's TC program assists Alberta innovators with the transfer of new ideas and scientific findings into successful commercial health-related products and services. TC funding often fills the gap when a commercially promising project does not fit the mandate of agencies that fund medical research and is not developed enough to attract outside investors.

Over the past 18 years, the TC program has funded 234 projects. Humphreys notes that AHFMR is currently monitoring 35 TC agreements. If all repay, there is a potential return of more than $10 million.

One of the companies that has repaid its TC funding is Edmonton-based Cytovax Biotechnologies Inc. Its $268,000 repayment stems from TC projects completed by Cytovax's predecessor company, Synthetic Peptides Inc. (SPI). SPI's technology was based on the pioneering work on synthetic peptides done by Dr. Robert Hodges, a biochemistry professor at the University of Alberta.

"Heritage funding was critical in the early stages of the development of the technology and the genesis of SPI," says Dr. Bin Huang, Cytovax President and CEO. "Without the early infusion of cash to keep development going within SPI, it could be that Cytovax would not exist today."

One of the companies that has repaid is Edmonton-based Cytovax Biotechnologies Inc.

We could end this story here—and it would look good. A grateful company, public money paid back, everyone happy. But it's not the end of the story, insists AHFMR's Humphreys.

"Repayment is a good step, but we're looking for something more in Alberta—knowledge workers employed, technologies that improve health, and a thriving biotech industry in the province," Humphreys says. "TC funding is only one component of what it takes to make this happen. For companies to achieve market success, help is required beyond the early-stage assistance of the TC program."

To illustrate her point, Humphreys points to Cytovax. The company's lead product, Cytovaxine, is designed to prevent one of the most common multi-drug-resistant "superbug" infections. The vaccine started in research in 1998 and has only now completed Phase 1 clinical trials; final data analysis is expected in September of this year.

"Drug development is a lengthy process," says Cytovax's Huang. "It's like a marathon." And a costly one, too. Cytovax's special warrant issue in 2000 and subsequent initial public offering in 2001 raised $18 million. In 2002, another $5.4 million was raised through private placement financing. This money is absolutely critical because Cytovax does not anticipate revenue from any commercial product for at least five years, until all phases of clinical trials for Cytovaxine are complete. Cytovax also has two other drug candidates under development, and plans to file Investigational New Drug (IND) applications for them in 2004.

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To keep its three main products moving along, Cytovax spent $5 million last year and expects to spend between $6 million and $7 million in 2004.

"Having enough money to keep development going continues to be an issue for us," says Huang. "We fall into a gap in financing. Venture capitalists are mainly interested in private companies, and Cytovax is publicly traded. On the other hand, we're at too early a stage to attract public investors. This is reflected in our stock price, which is very low despite our cash on hand and a solid product pipeline."

Companies supported by the TC program are showing signs of real progress.

Of course, Cytovax is not unique in this regard. Money problems are a fact of life in biotech, a situation that was neatly summarized in a story in the June 2, 2003, issue of Business Week:

> *Hundreds of small fry – the very companies that are laying the foundation for breakthroughs – are strapped for cash and shunned by investors who fear a dot-com-like crash. Big Pharma won't jump in to finance startups until they see positive late-stage trial results, and they're not willing to make oversize bets anymore. The top 10 biotech deals of 2002 were worth just $3 billion, down from $25 billion in 2001, according to PriceWaterhouseCoopers. VCs (venture capitalists) are staying away, too, because they're afraid they may never see a return on their investment.*

The article also notes that financing shortfalls are forcing many innovative young companies to license early-stage discoveries to larger companies, thus sacrificing potential profits. "This may happen to Cytovax too," says Huang. "We may be forced to partner early with a large pharmaceutical company, even though we want to keep our technology at least to Phase 2 trials. But if the funding situation becomes too difficult, we may be forced to give away the upside sooner."

Huang believes that more could be done in Alberta to help struggling technology companies. She notes that in Quebec, there are a number of venture capital funds that have a mandate to invest in Quebec companies. As well, provinces such as Quebec, Ontario, and British Columbia offer generous provincial incentives for R&D. "There are challenges to being in Alberta, and I think these should be looked at seriously," says Huang.

"I'm very proud of what Cytovax has accomplished. We have attracted substantial investment. We've gone from a handful of employees in the mid-1990s to 30 highly skilled staff members today. We're moving products forward, and with good fortune, we will be creating hundreds of millions of dollars in market capitalization. The rewards are big; that's why we're doing this. But there's still a long road ahead."

RIGHT: DR. BIN HUANG

TC snapshot

AHFMR's Technology Commercialization (TC) program assists Alberta innovators with the transfer of new ideas and scientific findings into successful commercial health products and processes. The program funds medical innovations demonstrating the potential to improve healthcare and be commercially successful. Basic research is not eligible, nor are product development projects; these are more appropriately funded by other mechanisms.

TC funding has three phases:

- **Phase 1** (maximum of $35,000) – exploring market and protecting intellectual property
- **Phase 2** (maximum $150,000) – testing technology and strengthening business case
- **Phase 3** (maximum $500,000) – implementing strategies and commercializing products

ARTICLE QUOTED: "Five Hurdles for Biotech" by Arlene Weintraub. BusinessWeek, June 2, 2003. pages 61-66.

The economics an

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ALBERTA'S HEALTHCARE SYSTEM is made up of a wide range of health programs and medical interventions, all competing for a limited amount of public funding. The system is also undergoing organizational change, from regionalization to restructuring of services. Given these two modern healthcare realities, how can funding be best used for maximum health benefits? And how can health professionals help bring about change that lets them give the best possible care? With AHFMR funding, Alberta researchers are using the theories and methods of economics and of organization change, to answer these crucial questions.

Dr. Alan Shiell, a Heritage Senior Health Scholar, explains that using economics in healthcare focuses mainly on the best effects of resource allocation within the healthcare system. Researchers studying the economics of the overall system are looking at such things as how hospitals function and how medical practitioners respond to different forms of payment for their services.

In the area of economic evaluation, researchers examine the costs of specific interventions, such as heart transplants, in relation to improved patient health outcomes. "We need to know how well an intervention works—what do we get for it and what does it cost?" says Dr. Shiell. His particular research area is the economics of health: the community-level interventions, broader policy, and societal influences on health outside of the formal health-care system.

Over the next five years, AHFMR funding will help Dr. Shiell and several research collaborators develop means of assessing the impact of community-lev' health interventions intended to promote population health. For example, the research team has started a two-year pilot project with a high school in an Alberta

"WHAT DO WE GET FOR IT AND WHAT DOES IT COST?"

d organization of hcare

rural community. The study is aimed at helping teens improve their health by reducing their risk-taking behaviour, and encouraging their sense of belonging to the school and the larger community. The researchers will also conduct large-scale evaluations of interventions at the community level. Once they get a better measure of the value of public health, the researchers will have information that can be used to improve the efficiency of public health, Dr. Shiell says. "We need the same standards of evidence applied to our practices as the people with whom we compete for resources."

THE RISK ADJUSTMENT MODEL CAN HELP DETERMINE WHICH REGION NEEDS THE MOST FUNDING

Heritage Population Health Investigator Dr. Mingshan Lu is exploring potential new ways of allocating funding to Alberta's health regions. "Resource allocation, economic incentives, and system efficiency are the central issues I'm looking at," she explains.

Alberta Health and Wellness currently provides annual block grants to health regions, based on each region's population in terms of age, sex, and socio-economic status. But this population-based formula only partly accounts for the health needs of people in each region and how various services are utilized, says Dr. Lu. She is investigating a new funding approach, developed in the last 10 years, called the risk adjustment model. It can help determine which region needs the most funding, based on the actual health status and clinical outcomes of people in each region. Along with collaborators at the universities of Calgary and Alberta and Boston University, Dr. Lu is looking at a "dynamic" risk adjustment model. This approach also includes financial incentives for regions that do a good job of keeping their populations healthy.

What dollar value would you place on rural ambulance services? How would you spend a limited amount of healthcare funding? Heritage Population Health Investigator Dr. Gillian Currie is testing a method from economic theory, called contingent valuation, for possible use in assessing how the public believes healthcare funding should be spent.

AHFMR funding will allow Dr. Currie to conduct a survey asking 300 people in the Calgary Health Region to rank hypothetical program expansions in heart care, cancer care, and ambulance services, and to assign a dollar value to each. "Assigning a dollar amount is a way for each individual to think about the things they would be willing to give up being able

ABOVE (L TO R): DRS. ALAN SHIELL, MINGSHAN LU AND GILLIAN CURRIE

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"Implementing system change is far from straightforward."

to consume or buy, as a way of expressing how much they value the health service or program expansion," she explains. The project also involves some tests of whether responses to the questions are consistent with theoretical predictions. Dr. Currie will do follow-up interviews to explore participants' reasons for how they ranked programs and assigned dollar values.

With support from the Eric Geddes/AHFMR Research Fellowship in Health Organization Studies, Dr. Karen Golden-Biddle and Professor Bob Hinings have spent three years examining change in Alberta's healthcare system. Professor Hinings says studies of organizational change in other sectors show that most proposed change actually doesn't get implemented. "So the issue becomes how to scope out the things that help to ensure successful implementation of change," he explains. "Implementing system change is far from straightforward," adds Dr. Golden-Biddle. "We're trying to identify and differentiate organizing practices that promote and sustain change."

Their study involved extensive data collection in Alberta health regions and examining four major system changes: province-wide regionalization; the introduction of the nurse practitioner; province-wide implementation of continuing care for the aging and disabled, as recommended in the 1999 report by MLA Dave Broda; and region-by-region innovations and experiments in delivering primary-care services.

Dr. Golden-Biddle and Professor Hinings are now publishing papers on the models and practices that ensure successful and sustained change. They also plan a two-year study that focuses directly on the human dimension of implementing system change.

"We discovered that some regions have systematic pockets of really good practices in implementing proposed change—hiring consultants to help build staff capability in managing change, encouraging staff input into resource allocation for training and education, and strengthening rather than downsizing middle management in order to translate new policies into action, for example," Dr. Golden-Biddle notes. "They are doing things which many people would like the whole system to do." rn

Dr. Alan Shiell is a Professor in the University of Calgary's Department of Community Health Sciences. An AHFMR Senior Scholar and Institute of Health Economics (IHE) Fellow, he and his research collaborators also receive funding from the Social Sciences and Humanities Research Council (SSHRC), the Canadian Institutes of Health Research (CIHR), and the Alberta Alcohol and Drug Abuse Commission (AADAC). Dr. Shiell is also a former faculty member for AHFMR's Swift Efficient Application of Research in Community Health (SEARCH) program.

Dr. Mingshan Lu is an Assistant Professor in the University of Calgary's Department of Economics and an Adjunct Assistant Professor in the Department of Community Health Sciences. She is an AHFMR Population Health Investigator, and IHE Fellow, and receives funding from the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness.

ABOVE (L TO R): DR. KAREN GOLDEN-BIDDLE AND PROFESSOR BOB HININGS

Eric Geddes/AHFMR Research Fellowship in Health Organization Studies

In September 2000, AHFMR committed $350,000 to help establish the Eric Geddes/AHFMR Research Fellowship in Health Organization Studies at the University of Alberta School of Business.

The fellowship honours the late Eric Geddes, one of the founders and the first chair of the AHFMR Board of Trustees. It is intended to help the School of Business attract and develop post-doctoral research excellence in health organization studies.■

Dr. Gillian Currie is an AHFMR Population Health Investigator and an Assistant Professor in the departments of Economics and Community Health Sciences at the University of Calgary. She is an IHE Fellow, and also receives funding from CIHR.

Bob Hinings is a Professor Emeritus in the University of Alberta's Faculty of Business. Dr. Karen Golden-Biddle is an Associate Professor in the Department of Strategic Management and Organization, and Director of Health Organization Studies in the University of Alberta's School of Business, as well as a faculty member for AHFMR's SEARCH program. Their three-year study is supported by the Eric Geddes/AHFMR Research Fellowship in Health Organization Studies, as well as the AHFMR Opportunity Fund and the Canadian Health Services Research Foundation.

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Hinings CR, Casebeer A, Reay T, Golden-Biddle K, Pablo A, Greenwood R. Regionalizing healthcare in Alberta: legislated change, uncertainty and loose coupling. *British Journal of Management*. In press.

The costs of hepatitis C

In the management of healthcare funding, it's crucial to know the costs of treatment and care for people with serious diseases. Yet decision-makers know little about the costs to Alberta's healthcare system of the liver disease hepatitis C. "We have only the most rudimentary information now," says Heritage-supported researcher Dr. Philip Jacobs. "We don't even know how much we're spending. But if decision-makers who allocate healthcare funding don't have a handle on costs, they really can't do a decent budgetary plan."

Dr. Jacobs' research will lead to a determination of the direct medical costs for individuals in the Capital Health region who are newly diagnosed with hepatitis C. More than 6,500 people in the Capital Health region tested positive for hepatitis C between 1995 and 2000. Keeping patient identity confidential throughout, the project will also assess the impact of interventions on costs. "We hope to arrive at a cost of the illness from the time that it's first reported until about four years after, for each person," says Dr. Jacobs.

Rough estimates of what it costs to treat and care for people with hepatitis C are currently based only on professional opinion, Dr. Jacobs explains. Actual costs, using data that exists in different formats and places within the healthcare system, have never been calculated. These costs could include physician services, hospitalization, new and often-expensive medications, and liver transplants. Costs also vary significantly depending on the stage of the disease.

With ethical approval for the study already secured, Dr. Jacobs expects the project to take about 1 1/2 years. Along with study partners Alberta Health and Wellness, the Capital Health Authority's Communicable Disease Control unit, and healthcare decision-makers, the research team will use the results to develop a more realistic model of budgetary planning for hepatitis C and its health impacts. "Better planning would improve everybody's healthcare," says Dr. Jacobs.

ABOVE: DR. PHILIP JACOBS

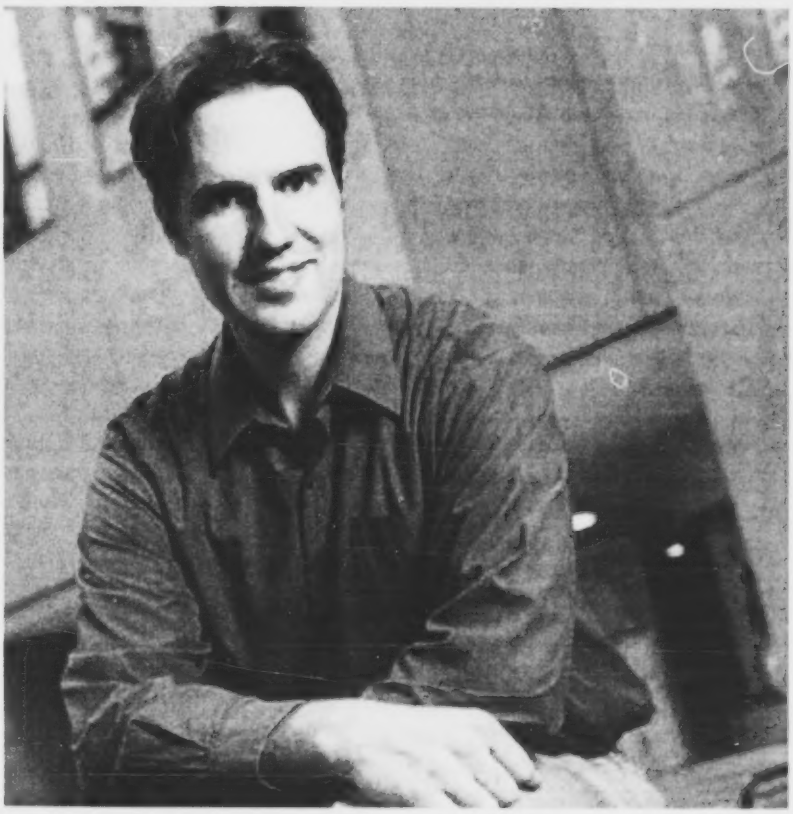
Dr. Philip Jacobs is a Professor in the Department of Public Health Sciences at the University of Alberta and an Institute of Health Economics Fellow. He receives support for his study from the Health Research Fund, which is administered by AHFMR on behalf of Alberta Health and Wellness. Dr. Jacobs is also a former faculty member for AHFMR's SEARCH program.

Selected publications

Jacobs P, Ng YC, Stafinski T, Dodd RY, Larke B, Wong W. Labor force participation among individuals with hepatitis C in the United States. *PharmacoEconomics*. In press.

Creating a lot of nerve

We humans have a central nervous system (CNS), which includes the brain, cranial nerves, and spinal cord. We also have a peripheral nervous system, which includes the nerves that link the CNS with the eyes and sensory organs, muscles, blood vessels, and glands in our body. Peripheral nerves are involved in motor activity such as walking, and they also carry back to the CNS sensory information such as the feeling of the sun's heat on our skin. Peripheral nerves, especially those in the arms and legs, which have little protection, are very vulnerable to injury. Acute peripheral nerve injuries can result from a broken leg, a car accident, being shot or stabbed—anything where one of the peripheral nerves is severed. Chronic peripheral nerve injury can occur with conditions like diabetes.



DAVID MCDONALD

Surgeons operating through microscopes can repair the tiniest parts of the body, including severed nerve endings. But with the peripheral nervous system, even a stitch in time may not restore full function. "Even though we have excellent microsurgeons and very good techniques and tools, the functional recovery is often poor," says David McDonald, AHFMR Student and Ph.D. candidate in the University of Calgary's Department of Clinical Neurosciences.

Fortunately, peripheral nerves have the amazing capacity to naturally "regrow" (regenerate) to a limited degree after being cut, crushed, or otherwise seriously injured. While researchers have studied this regrowth mainly in the laboratory, using cultured nerve tissue, David has developed a new model to study peripheral nerve regeneration. "Our model is the first of its kind that seems to be able to work very well," he says.

When studying the effects of chemical agents on peripheral nerve regeneration, previous models have required many applications of the chemical onto the injured nerve. McDonald's new model uses a microinjection port that is connected via a catheter to a silicone chamber encompassing the damaged nerve. This allows researchers to inject agents that promote or slow regeneration directly onto an isolated severed sciatic nerve. "This model is a direct way of measuring the local effects of these nerve regeneration-altering

agents," McDonald says. "We can put in whatever agents we want, whenever we want."

The impact of various chemicals, such as nitric oxide or growth factors, is assessed by using a microscope to count the number of regenerated nerve fibres and measure their size in the healing nerve. Another device measures nerve conduction velocity—how fast the sensory and motor nerves conduct electrochemical impulses. David explains that a better understanding of the factors that promote or hinder peripheral nerve regeneration may lead to the development of new drugs that would encourage regeneration and improve functional recovery in people with nerve injuries.

David plans to complete his Ph.D. this fall, and then go on to medical school to prepare for a career as a clinician researcher.

David McDonald is an AHFMR Student and a Ph.D. candidate in the University of Calgary's Department of Clinical Neurosciences under the supervision of Heritage Senior Scholar Dr. Douglas Zochodne.

Selected publication

McDonald DS, Zochodne DW. An injectable nerve regeneration chamber for studies of unstable soluble growth factors. *Journal of Neuroscience Methods* 2003 Jan;122(2):171-178.

DR. STEPHEN ROBBINS

The spring 2003 story "New tools in the fight against cancer" incorrectly identified a photo of Dr. Dallan Young as Dr. Stephen Robbins.

Dr. Robbins is a cancer researcher and Heritage Senior Scholar. In addition to his research into how cells communicate with one another, he also works on molecular profiling at the University of Calgary's Southern Alberta Microarray Facility. Molecular profiling is expected to have great value in more accurately determining how best to treat cancer patients. Dr. Robbins explains that knowing the molecular profile would allow doctors to treat those cancerous tumours that are more likely to relapse with more aggressive therapies.

Dr. Dallan Young is a Professor in the Departments of Biochemistry and Molecular Biology, and Oncology at the University of Calgary. He studies basic mechanisms that control cell growth, repair damaged DNA, and regulate how genes are turned "on" and "off". Such mechanisms are often the targets of genetic mutations associated with cancer and other diseases. Dr. Young's studies will help in understanding what goes wrong in cancer cells, and could lead to the development of better cancer therapies. •

Research views

Making connections for research

Medical genetics—a very fundamental level

Genetic mapmaking

Restoring movement after nerve injury

A milestone for technology commercialization

The economics and organization of healthcare

The costs of hep C

Heritage Youth Researcher Summer (HYRS) Program 2003

The opportunity to do hands-on biomedical research was what caught Naeem's interest about the Heritage Youth Researcher Summer (HYRS) program. HYRS participants spend six weeks working under the supervision and mentorship of university researchers, the majority of whom are AHFMR-funded. The program is run at the University of Alberta, the University of Calgary, and the University of Lethbridge. It is open to exceptional Grade 11 students across the province.

Naeem, who attends Edmonton's McNally High School, says that math has been his strongest subject since junior high. However, a Grade 10 biology course sparked a strong interest in human physiology and biomedicine, the application of biology to clinical medicine. "So I'm sort of torn between the physical sciences and the biological sciences. I think the HYRS program will help me in resolving my career direction.

"Beyond that, this is really an amazing opportunity—to job-shadow a researcher, see what goes on in a lab, get a feeling for what the life of a researcher is really like. Even if I don't go on to become a researcher, I think this will be a life-lasting experience."

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In July, Naeem began working in Heritage Scientist Dr. Gary Lopaschuk's lab at the University of Alberta. Dr. Lopaschuk is internationally recognized for his research on energy metabolism in the heart. He has participated in the HYRS program for the past two years. "HYRS students are eager and keen to learn," he says. "It is a very rewarding experience training these young scientists."

Naeem is one of 45 high-school students participating in the 2003 HYRS program. More than 190 students applied to the program, representing 95 schools throughout the province. To qualify for HYRS, students must have an 85% average in the required math and science subjects, obtain two teacher references, and write an essay on an assigned topic. Applications are judged by a committee of three teachers and two HYRS managers.

For more information about the HYRS program, please check the AHFMR Web site at www.ahfmr.ab.ca and click on "For Students".

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